REMARKS

Status of the claims

Claims 28-35 and 59-61 are pending in the application. Claims 28, 30, 31, 32, 33, 34, 35, 60 and 61 are currently amended. Claim 29 is herein canceled. Claims 1-27, and 36-58 were previously canceled. Claims 28-35 and 59-60 are rejected. Claim 61 is objected to.

Claim amendments

Claims 28, 30, 31, 32, 33, 34, 35, 60 and 61 are amended to overcome rejection under 35 U.S.C. §102(e). Claims 28, 29, 30, 31, 32, 33, 34, 35, 60 and 61 are amended to clarify that the sequence of the reporter linker is universal (generic linkers) or in other words these sequences are selected such that they will not hybridize to any target sequence and can be used to prepare any number of probes. Claim 28 is further amended to clarify the design of a wrap probe used in the method of claim 28. Amended claim 28 recites a probe unit comprising two oligonucleotides that are overlapped end to end to form a linear probe unit prior to target hybridization. The first oligonucleotide comprises three segments sequentially: a first universal probe linker on one end that hybridizes to a universal reporter linker of a reporter, a central sequence complementary to the single-stranded target nucleotide sequence, and an overlap linker on the other end. The second oligonucleotide comprises two segments sequentially: a matching overlap linker that is hybridized to the overlap

linker of the first oligonucleotide, and a second universal probe linker. Claim 29 is canceled, as the subject matter of this claim is included in claim 28. Claim 61 is further amended to delete non-elected subject matter.

Applicant respectfully requests that the finality of the restriction to SEQ ID NO: 76 with respect to the universal reporter linker be withdrawn. Applicant submits that the invention will not work if the universal linker is restricted to one nucleotide sequence. At the very least, two complementary sequences are needed to connect single linker reporters to the WRAP probe unit of Claim 28. To work with a multilinker or any array of reporters, a minimum of 4 universal sequences are needed (claims 32, 33, 34, 35). Thus the claimed invention will not work with just one universal linker. Accordingly Applicants respectfully request that the restriction of the invention to universal linker of SEQ ID No: 76 be withdrawn.

Claim Objections

Claim 61 is objected to as being dependent upon a rejected base claim and also because the claim incorporates non elected subject matter. Claim 61 is amended to delete non-elected subject matter. The arguments presented infra clearly show that claim 28 is not anticipated or obvious over prior art. Thus claim 61 is not dependent from a base claim that contains subject matter that is anticipated or obvious over prior art. Accordingly, Applicant respectfully requests that the objection to claim 61 be withdrawn.

Claim rejection under 35 U.S.C. § 102(e)

Claim 28 is rejected under 35 U.S.C. § 102(e) as being anticipated by **Zhang** et al. (U.S. patent 5,876,924). Applicant respectfully traverses this rejection.

The Examiner states that **Zhang** et al. teach the method of detecting target nucleotide as recited in claim 28 of the instant application. The Examiner further states that **Zhang** et al. teach a nucleic acid probe with a central sequence complementary to the target sequence and which further comprises a probe linker at each terminal end such that each probe linker comprises a single stranded nucleotide sequence that does not hybridize to the target sequence (figure 6, column 41, example 7). Applicant respectfully disagrees.

Applicant submits that **Zhang** et al. primarily teach hybridizing a target nucleic acid to several non-overlapping oligonucleotide probes that hybridize to adjacent regions in the target nucleic acid. The probes are then ligated to form a continuous sequence, which is then amplified to determine the presence of the target nucleic acid (Abstract). In one embodiment **Zhang** et al. teach the detection of target nucleic acid, which precludes the use of a ligation step. In this approach **Zhang** et al. use a probe with a central sequence that is complementary to the target nucleic acid, which is flanked by single stranded nucleotide sequences that do not hybridize to the target sequence. These flanking sequences bind primers for amplification of the probe (Figure 6, example 7).

Applicant has amended claim 28 to clarify that the reporter linkers used in the instant method are universal linkers ('generic linker sequences" as described in the specification. These sequences are checked against GenBank

sequences and do not show complementarity to known natural sequences). **Zhang** et al. do not teach or suggest that the primer binding sequence flanking the target binding sequences are universal and that they may be used to generate any number of probes. Furthermore, Applicant's method uses labeled reporters with universal reporter linkers to detect the presence of target nucleic acid sequences. So the instant method does not require an amplification step as is required in the method by **Zhang** et al.

Applicant has further amended claim 28 to include a probe unit such that this probe comprises two partially overlapping oligonucleotides such that the first oligonucleotide comprises three segments sequentially: a first universal probe linker on one end that hybridizes to a universal reporter linker of a reporter, a central sequence complementary to the single-stranded target nucleotide sequence, and an overlap linker on the other end. The second oligonucleotide comprises two segments sequentially: a matching overlap linker that is hybridized to the overlap linker of the first oligonucleotide, and a second universal probe linker. This probe design specifically considers the sequence of reporter linkers that can bind to the two probe linkers (complementary reporter linkers). **Zhang** et al. does not anticipate the use of such a probe unit to detect target nucleic acids as **Zhang** et al. does not anticipate the use of reporters on both ends of the probe as is taught only in the Applicant's invention.

At minimum absent a teaching of the use of reporters with universal reporter linkers and the specific probe composition as described in amended claim 28, **Zhang** et al. does not anticipate claim 28. Accordingly Applicant

respectfully requests that the rejection of claim 28 under 35 U.S.C. § 102(e) as being anticipated by **Zhang** et al. be withdrawn.

Claim rejection under 35 U.S.C. § 103(a)

Claims 29-35 and 59-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Zhang** et al (U.S. Patent 5, 876, 924) in view of **Urdea** et al. (U.S. Patent 5, 681, 697). Applicant respectfully traverses this rejection.

The Examiner states that **Zhang** et al. teach all aspects of independent claim 28 except for use of Nucleic acid reporter arrays. The Examiner also states that **Urdea** et al. overcome this deficiency by teaching the use of reporter arrays to amplify signals for target detection. The Examiner also states that **Urdea** et al. teach a first terminal probe linker and a second terminal probe linker (see figure 16, where LE has an X and Y region that hybridizes to the Amp 1 probe). Applicant respectfully disagrees.

Urdea et al. only teach using a probe with one terminal probe linker (see the Reponse {pg 14-15} filed February 11, 2005, for the Office Action of October 28, 2004). **Zhang** et al. and the Applicant's invention are as described supra. Applicant submits that as described *supra* amended claim 28 is novel and non obvious over **Zhang** et al. The teaching by **Urdea** et al. does not remedy the deficiency in **Zhang** et al. **Urdea** et al. does not teach the probe composition used in the Applicant's method or the use of universal reporter linker sequences. Thus a combination of **Zhang** et al. and **Urdea** et al. does not make claim 28 obvious. Claim 29 is herein canceled. Claims 30-35 and 59-60 depend either directly or

indirectly from amended claim 28. As claim 28 is novel and non obvious over **Zhang** et al. and **Urdea** et al., it follows that dependent claims 30-35 and 59-60 are also novel and non-obvious over this prior art. Thus, the Examiner's arguments with respect to rejection of claims 29-35 and 59-60 under 35 U.S.C. 103(a) as being unpatentable over **Zhang** et al (U.S. Patent 5, 876, 924) in view of **Urdea** et al. (U.S. Patent 5, 681, 697) are moot in view of the claim amendments. Accordingly Applicant respectfully requests that the rejection of claims 29-35 and 59-60 under 35 U.S.C. 103(a) be withdrawn.

This is intended to be a complete response to the Final Office Action mailed October 28, 2005. Applicant submits that the pending claims 28, 30-35 and 59-60 are in condition for allowance and respectfully requests that these claims be passed to issuance. If any issues remain outstanding, please telephone the undersigned attorney of record for immediate resolution. Please debit any insufficiency in the fees from Deposit Account No. 07-1185 upon which the undersigned is allowed to draw.

Respectfully submitted,

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